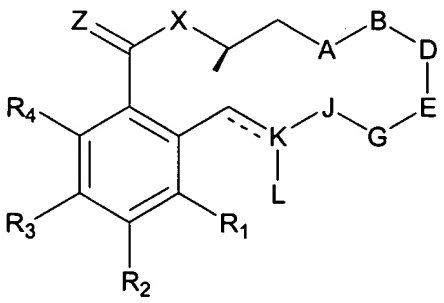
Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

1. (Currently amended) A compound having the structure:



wherein the dotted line --- represents ~~a~~ an optional bond, ~~whereby a~~ such that either a single or a double bond is present~~, or the dotted line --- is absent, whereby a single bond is present~~;

R_1 is hydrogen, halogen, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or $N(R_A)_2$, wherein each occurrence of R_A is independently hydrogen, ~~a protecting group,~~ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety;

R_2 is hydrogen, halogen, cyano, $-OR_B$, $-N(R_B)_2$, $-SR_B$, $-O(C=O)R_B$, $-N(R_B)(C=O)(R_B)$, $-C(O)R_B$, $-C(O)OR_B$, $-CON(R_B)_2$, $-OCO_2R_B$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_B is independently hydrogen, ~~a protecting group~~ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety;

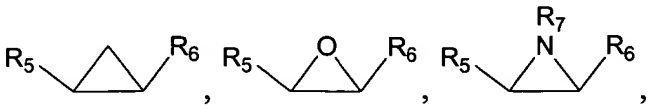
R_3 is hydrogen, halogen, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or $-N(R_C)_2$, wherein each occurrence of R_C is independently hydrogen, ~~a protecting group,~~ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl

moiety;

R_4 is hydrogen, halogen, cyano, $-OR_D$, $-N(R_D)_2$, $-SR_D$, $-O(C=O)R_D$, $-N(R_D)(C=O)(R_D)$, $-C(O)R_D$, $-C(O)OR_D$, $-CON(R_D)_2$, $-OCO_2R_D$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_D is independently hydrogen, ~~a protecting group~~ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety;

Z is ~~O, S or NR_E, wherein R_E is hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or OR_F, wherein R_F is hydrogen, a protecting group, an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety~~;

X is ~~O, S or NR_G, wherein R_G is hydrogen or lower alkyl~~;

A and B together represent 

, $-CHR_5-CHR_6-$, $-CR_5=CR_6-$, wherein R_5 and R_6 are each independently hydrogen, halogen, cyano, $-OR_J$, $-N(R_J)_2$, $-SR_J$, $-O(C=O)R_J$, $-O(S=O)R_J$,$-N(R_J)(C=O)(R_J)$, $-C(=O)R_J$, $-C(=O)OR_J$, $-CON(R_J)_2$, $-OCO_2R_J$, ~~$-OS(=O)OR_J$~~ $\underline{-OSO_2R_J}$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_J is independently hydrogen, ~~a protecting group,~~ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and wherein R_7 is hydrogen, ~~a protecting group,~~ $-OR_K$, $-SR_K$, $-C(O)OR_K$, ~~$-C(O)NR_K$~~, $-S(O)_2R_K$, $-O(C=O)R_K$, $-N(R_K)(C=O)(R_K)$, $-C(O)R_K$, $-C(O)OR_K$, $-CON(R_K)_2$, $-OCO_2R_K$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_K is independently hydrogen, ~~a protecting group~~ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or when A and B together represent $-CHR_5-CHR_6-$, R_5 and R_6 taken together represent a substituted or unsubstituted 3-7 membered aliphatic, heteroaliphatic, aryl or heteroaryl ring,

D and E together represent $-CHR_8-CHR_9-$, $-CR_8=CR_9-$, wherein R_8 and R_9 are each independently hydrogen or lower alkyl;

G and J together represent $-CHR_{10}-CHR_{11}-$, $-CR_{10}=CR_{11}-$, wherein R_{10} and R_{11} are each

independently hydrogen or lower alkyl;

K and L together represent C=O, C=S, CH-CH_3, CH-$CH(R_L)_2$, C=$C(R_L)_2$, -CH_2-, -C(-$S(CH_2)_3S$-)-, CH-OR_L, CH-SR_L, CH-$N(R_L)_2$, CH-$N(R_L)(C=O)(R_L)$, C=N-O-R_L, CH-N=O, C=$C(R_L)$-$N(R_L)_2$, C=N-R_L, C=N-$N(R_L)_2$, or, if the dotted line --- represents a bond, whereby a double bond is present, then K and L together represent C-$N(R_L)_2$, wherein each occurrence of R_L is independently hydrogen, ~~a protecting group,~~ an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or two occurrences of R_L taken together represent a 3 to 7-membered cyclic aliphatic, heteroaliphatic, aromatic or heteroaromatic moiety;

whereby each of the foregoing aliphatic and heteroaliphatic moieties may independently be substituted or unsubstituted, cyclic or acyclic, or branched or unbranched, and each aryl, heteroaryl, alkylaryl, and alkylheteroaryl moiety may be substituted or unsubstituted;

wherein one or any two of R_1, R_A, R_2, R_B, R_3, R_C, R_4, R_D, R_5, R_6, R_J, or R_L are optionally a linker covalently bonded to a compound selected from the group consisting of radicicol, monocillin, ~~analogues of radicicol and monocillin,~~ geldanamycin, ~~analogues of geldanamycin,~~ and steroids; and

pharmaceutically acceptable derivatives thereof,

with the proviso that:

(1) ~~if Z is O; if X is O;~~ if A and B together are  and R_5 and R_6 are each hydrogen; if D and E together are –CH=CH-; if G and J together are -CH=CH-; if K and L together are C=O; if R_1 is hydrogen or Cl; and if R_3 is hydrogen,

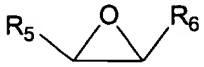
then R_2 is not -OR_B or -O(C=O)R_B, wherein R_B is hydrogen or an alkyl, alkoxy, alkenyl, alkenyloxy, alkynyl, aryl, aryloxy, heterocycle, cycloalkyl, cycloalkenyl, or cycloalkenyl fused to an aryl group; and R_4 is not -OR_D or -O(C=O)R_D, wherein R_D is hydrogen or an alkyl, alkoxy, alkenyl, alkenyloxy, alkynyl, aryl, aryloxy, heterocycle, cycloalkyl, cycloalkenyl, or cycloalkenyl fused to an aryl group;

(2) if A and B together are  and R_5 and R_6 are each hydrogen; if D and E

together are $-CH_2-CH_2-$; if G and J together are $-CH_2-CH_2-$; if K and L together are C=O; if R_1 is Cl; and if R_3 is hydrogen,

then R_2 is not $-OR_B$ or $-O(C=O)R_B$, wherein R_B is hydrogen or an alkyl, alkoxy, alkenyl, alkenyloxy, alkynyl, aryl, aryloxy, heterocycle, cycloalkyl, cycloalkenyl, or cycloalkenyl fused to an aryl group; and R_4 is not $-OR_D$ or $-O(C=O)R_D$, wherein R_D is hydrogen or an alkyl, alkoxy, alkenyl, alkenyloxy, alkynyl, aryl, aryloxy, heterocycle, cycloalkyl, cycloalkenyl, or cycloalkenyl fused to an aryl group; and

(3) ~~if Z is O; if X is O,~~ if R_1 is Cl; if R_2 is OR_A and R_A is hydrogen, alkanoyl, alkenoyl, tert-butyl dimethylsilyl or tert-butyldiphenylsilyl; if R_3 is hydrogen; if R_4 is OR_B and R_B is hydrogen, alkanoyl, alkenoyl, tert-butyldimethylsilyl, or tert-butyldiphenylsilyl; if D and E together are –CH=CH-; if G and J together are -CH=CH-; if A and B together are



or if A and B together are $-CHR_5-CHR_6-$ and R_6 is halogen and R_5 is OR_J, wherein R_J is hydrogen, alkanoyl, or alkenoyl, or R_5 is $-O(S=O)R_J$, wherein R_J is a second compound of formula (I) linked via an oxygen atom present at R_5 in the second compound, and wherein R_6 is halogen; Z is O; X is O, R_1 is Cl; R_2 is OR_A and R_A is hydrogen, alkanoyl, alkenoyl, tert-butyl dimethylsilyl or tert-butyldiphenylsilyl; R_3 is hydrogen; R_4 is OR_B and R_B is hydrogen, alkanoyl, alkenoyl, tert-butyldimethylsilyl, or tert-butyldiphenylsilyl;

then K and L together are not C=O or C=N-O-R_L, when R_L is hydrogen, or substituted or unsubstituted lower alkyl, a substituted or unsubstituted ~~alkylene~~ alkenyl moiety, a substituted ~~carbonyl~~ ~~acyl~~ moiety or a substituted or unsubstituted aryl moiety;

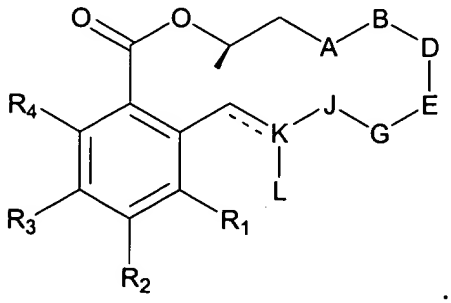
except that K and L together can be C=N-O-R_L, when R_L is a linker covalently bonded to a compound selected from the group consisting of radicicol, monocillin, ~~analogues of radicicol and monocillin,~~ geldanamycin, ~~analogues of geldanamycin,~~ and steroids~~; or~~.

2. (Currently amended) The ~~method~~ compound of claim 1, wherein one or any two of R_1, R_A, R_2, R_B, R_3, R_C, R_4, R_D, R_5, R_6, R_J, or R_L are a linker covalently bonded to a compound selected from the group consisting of radicicol, monocillin, ~~analogues of radicicol and~~

~~monocillin,~~ geldanamycin, ~~analogues of geldanamycin,~~ and steroids, wherein the linker is an aliphatic or heteroaliphatic moiety, whereby said aliphatic or heteroaliphatic moiety is substituted or unsubstituted, branched or unbranched, or cyclic or acyclic.

3. (Currently amended) The ~~method~~ compound of claim 1, wherein one or any two of R_1, R_A, R_2, R_B, R_3, R_C, R_4, R_D, R_5, R_6, R_J, or R_L are a linker covalently bonded to a compound selected from the group consisting of radicicol, monocillin, ~~analogues of radicicol and monocillin,~~ geldanamycin, ~~analogues of geldanamycin,~~ and steroids, wherein the linker is a moiety having one of the structures $-(CH_2)_n-CH=CH-(CH_2)_m-$, $-(CH_2)_p-C\equiv C-(CH_2)_q-$, or $-CH_2(CH_2)_sCH_2-$, wherein each occurrence of n, m, p, q and s is independently an integer from 0-10, and wherein one or more of the hydrogen atoms are optionally replaced with an alkyl, heteroalkyl, aryl, heteroaryl, alkylaryl or alkylheteroaryl moiety or a secondary or tertiary amine, hydroxyl, or thiol.

4. (Original) The compound of claim 1, wherein Z and X are each O, and the compound has the structure:

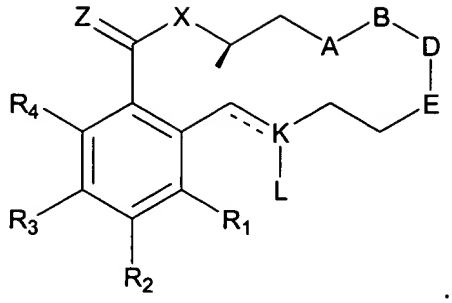


5. (Canceled)

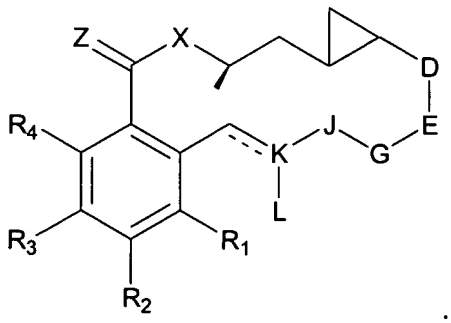
6. (Canceled)

7. (Original) The compound of claim 1, wherein G and J together represent $-CH_2-CH_2-$

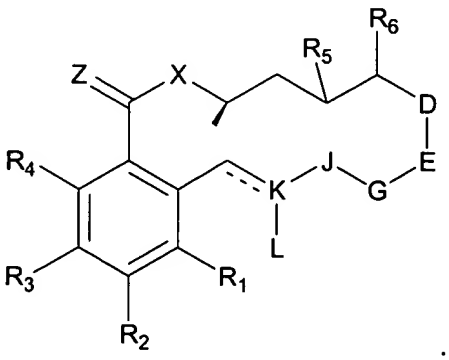
and the compound has the structure:



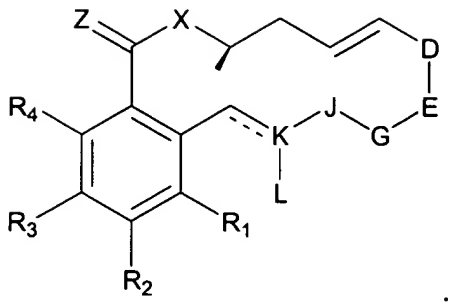
8. (Original) The compound of claim 1, wherein A-B is a cyclopropyl ring and the compound has the structure:



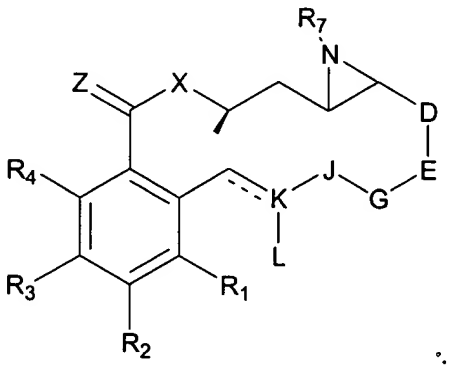
9. (Original) The compound of claim 1, wherein A and B together represent -CHR_5-CHR_6- and the compound has the structure:



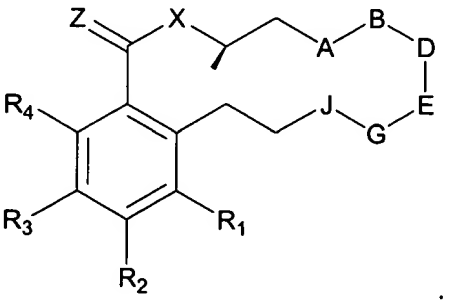
10. (Original) The compound of claim 1, wherein A and B together represent -CH=CH- and the compound has the structure:



11. (Original) The compound of claim 1, wherein A and B together represent an aziridine and the compound has the structure:

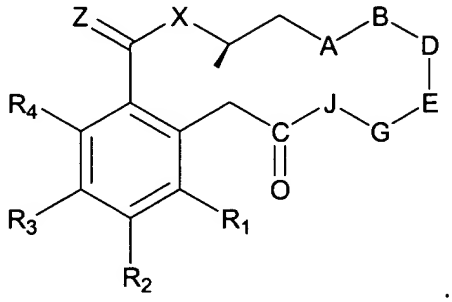


12. (Currently amended) The compound of claim 1, wherein the optional bond represented by the dotted line --- is absent ~~whereby~~ so that a single bond is present, K and L together represent -CH_2- and the compound has the structure:

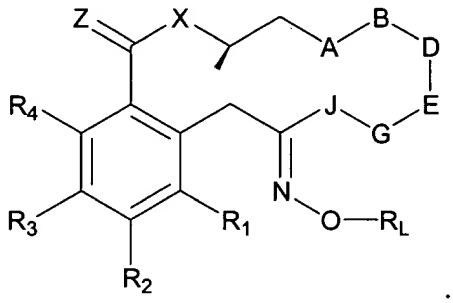


13. (Currently amended) The compound of claim 1, wherein the optional bond represented

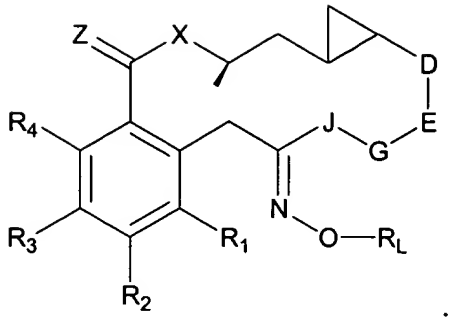
by the dotted line --- is absent ~~whereby~~ so that a single bond is present, K-L together represent C=O and the compound has the structure:



14. (Currently amended) The compound of claim 1, wherein the optional bond represented by the dotted line --- is absent ~~whereby~~ so that a single bond is present, K and L together represent C=N-O-R_L and the compound has the structure:

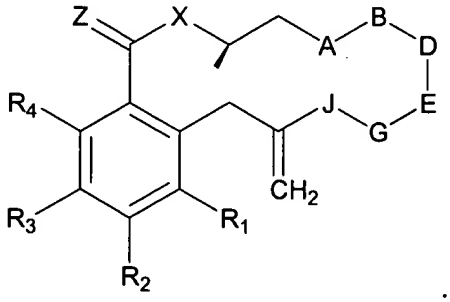


15. (Currently amended) The compound of claim 1, wherein the optional bond represented by the dotted line --- is absent ~~whereby~~ so that a single bond is present, A and B together represent a cyclopropyl group, K and L together represent C=N-O-R_L and the compound has the structure:

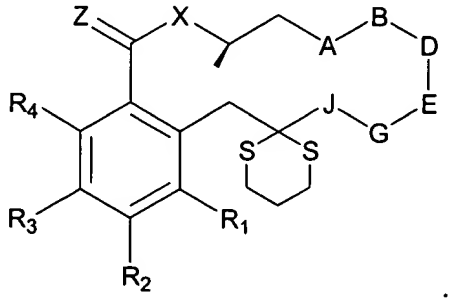


16. (Currently amended)

The compound of claim 1, wherein the optional bond represented by the dotted line --- is absent ~~whereby~~ so that a single bond is present, K and L together represent $C{=}CH_2$ and the compound has the structure:

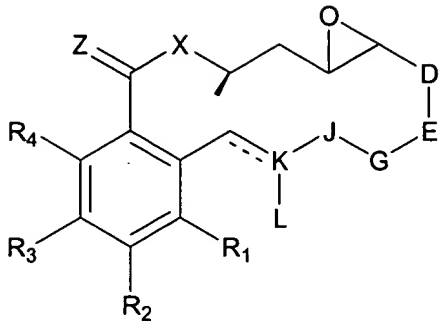


17. (Currently amended) The compound of claim 1, wherein the optional bond represented by the dotted line --- is absent ~~whereby~~ so that a single bond is present, K and L together represent a dithiane, $-C(-S(CH_2)_3S-)-$, and the compound has the structure:



18. (Currently amended) The compound of claim 1, wherein A and B together represent an

epoxide and the compound has the structure:



~~wherein if Z is O and X is O, then~~ at least one of the D-E, G-J, K-L, R_2 and R_4 are defined as:

R_2 is hydrogen, halogen, cyano, $-N(R_B)_2$, $-SR_B$, $-N(R_B)(C=O)(R_B)$; $-C(O)R_B$, $-C(O)OR_B$, $-CON(R_B)_2$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_B is independently hydrogen, ~~a protecting group~~ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety;

R_3 is not hydrogen;

R_4 is hydrogen, halogen, cyano, $-N(R_D)_2$, $-SR_D$, $-N(R_D)(C=O)(R_D)$, $-C(O)R_D$, $-C(O)OR_D$, $-CON(R_D)_2$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, wherein each occurrence of R_D is independently hydrogen, ~~a protecting group~~ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety;

D and E together represent $-CHR_8-CHR_9-$ wherein R_8 and R_9 are each independently hydrogen or lower alkyl;

G and J together represent $-CHR_{10}-CHR_{11}-$, wherein R_{10} and R_{11} are each independently hydrogen or lower alkyl;

K and L together represent C=S, $CH-CH_3$, $CH-CH(R_L)_2$, $C=C(R_L)_2$, $-CH_2-$, $-C(-S(CH_2)_3S-)-$, $CH-OR_L$, $CH-SR_L$, $CH-N(R_L)_2$, $CH-N(R_L)(C=O)(R_L)$, CH-N=O, $C=C(R_L)-N(R_L)_2$, $C=N-R_L$, $C=N-N(R_L)_2$, or, if the optional bond represented by the dotted line --- ~~represents a bond, whereby~~ is present so that a double bond is present, then K and L together represent $C-N(R_L)_2$, wherein each occurrence of R_L is independently hydrogen, ~~a protecting~~

~~group,~~ an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or two occurrences of R_L taken together represent a 3 to 7-membered cyclic aliphatic, heteroaliphatic, aromatic or heteroaromatic moiety; or

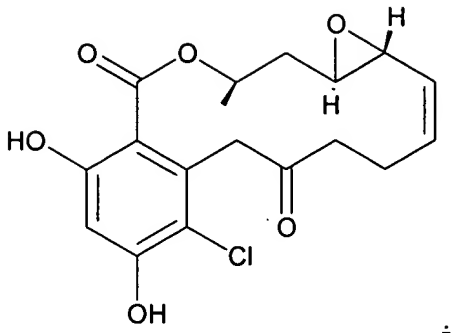
any two of R_1, R_A, R_2, R_B, R_3, R_C, R_4, R_D, R_5, R_6, R_J, or R_L are a linker covalently bonded to a compound selected from the group consisting of radicicol, monocillin, ~~analogues of radicicol and monocillin,~~ geldanamycin, ~~analogues of geldanamycin,~~ and steroids.

19. (Currently amended) The compound of claim 1, wherein A and B together are $-CHR_5-CHR_6-$ or $-CR_5=CR_6-$ and R_5 and R_6 are each independently hydrogen, halogen, cyano, $-OR_J$, $-N(R_J)_2$, $-SR_J$, $-O(C=O)R_J$, $O(S=O)R_J$,$-N(R_J)(C=O)(R_J)$, $-OCO_2R_J$ or $-OSO_2R_J$ and each occurrence of R_J is independently hydrogen, ~~a protecting group~~ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety.

20. (Original) The compound of claim 19, wherein R_5 and R_6 are each independently hydrogen, or lower alkyl.

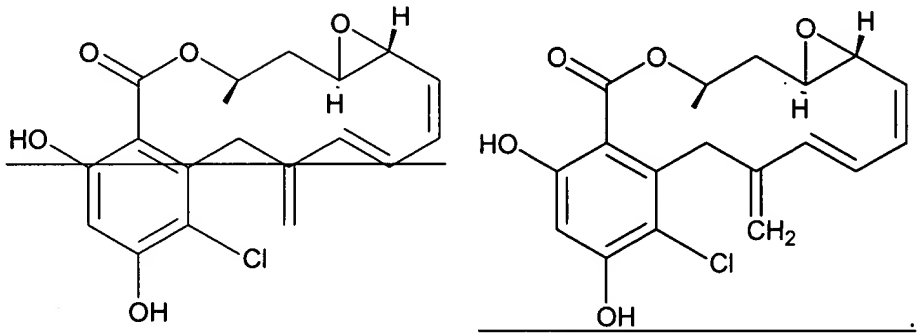
21. (Currently amended) The compound of claim 1, wherein R_1 and R_3 are each independently halogen, hydrogen, or lower alkyl; R_2 is hydrogen or $-OR_B$, wherein each occurrence of R_B is independently hydrogen, ~~a protecting group~~ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, and R_4 is hydrogen or $-OR_D$, wherein each occurrence of R_D is independently hydrogen, ~~a protecting group~~ or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety.

22. (Currently amended) The compound of claim 1, wherein the compound has the structure:

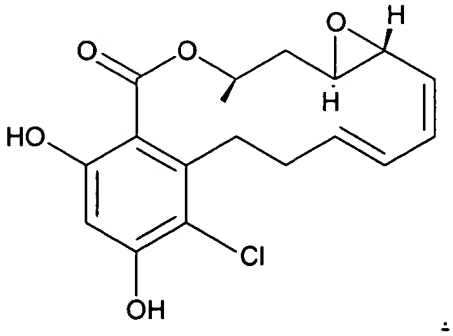


23. (Canceled)

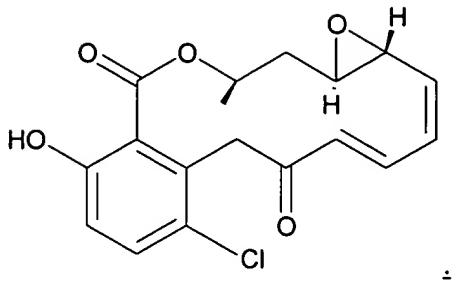
24. (Currently amended) The compound of claim 1, wherein the compound has the structure:



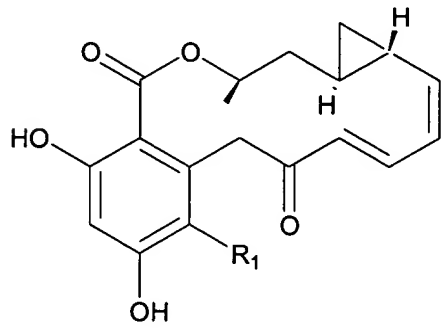
25. (Currently amended) The compound of claim 1, wherein the compound has the structure:



26. (Currently amended) The compound of claim 1, wherein the compound has the structure:

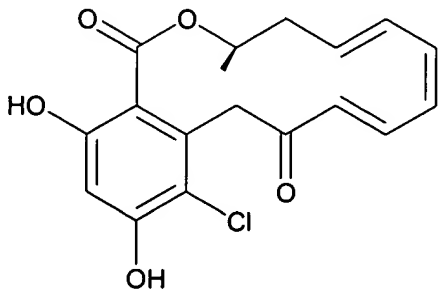


27. (Original) The compound of claim 1, wherein the compound has the structure:



wherein R_1 is hydrogen or Cl.

28. (Original) The compound of claim 1, wherein the compound has the structure:



29. (Canceled)

30. A pharmaceutical composition for treating Hsp90-dependent cancers comprising a compound of claim 1 and a pharmaceutically acceptable carrier.

31. (Canceled)

32. (Canceled)

33. (Currently amended) A method for treating an Hsp90-dependent cancer comprising:

administering a therapeutically effective amount of a compound of claim 1 to a subject in need thereof.

34. (Original) The method of claim 33, wherein the therapeutically effective amount is in the range of 0.001 mg/kg to 50 mg/kg of body weight.

35. (Original) The method of claim 33, wherein the therapeutically effective amount is in the range of 0.01 mg/kg to about 25 mg/kg of body weight.

36. (Canceled)

37. (Canceled)

38. (Currently amended) A method for inhibiting the growth of or killing Hsp90-dependent cancer cells, said method comprising:

contacting Hsp90-dependent cancer cells with an amount of a compound of claim 1 effective to inhibit the growth of or kill the cancer cells.

39. (Canceled)

40. (Canceled)

41. (Canceled)

42. (Canceled)

43. (Canceled)

44. (Canceled)

45. (Canceled)

46. (Canceled)

47. (Canceled)

48. (Canceled)

49. (Canceled)

50. (Canceled)

51. (Canceled)

52. (Canceled)

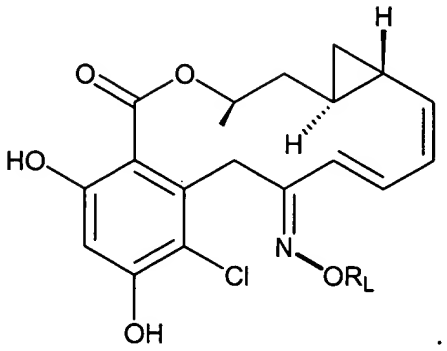
53. (Canceled)

54. (Canceled)

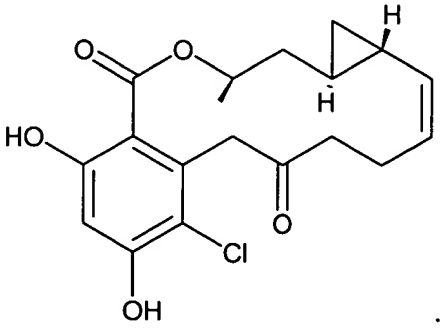
55. (Canceled)

56. (Canceled)

57. (New) The compound of claim 1, wherein the compound has the structure:



58. (New) The compound of claim 1, wherein the compound has the structure:



59. (New) A method for inhibiting the growth of or killing cancer cells that do not express retinobalstoma (Rb^- cancer cells), said method comprising:

contacting Rb^- cancer cells with an amount of a compound of claim 1 effective to inhibit the growth of or kill the cancer cells

60. (New) A method for inhibiting the growth of or killing cancer cells that do not express retinobalstoma (Rb^- cancer cells), said method comprising:

contacting the cancer cells with an amount of a compound of claim 1 effective to inhibit the growth of or kill Rb^- cancer cells.

61. (New) The method of claim 59 or 60, wherein the cancer cells are selected from the group consisting of small-cell carcinoma cells, glioblastoma cells, and retinoblastoma cells.

62. (New) The method of claim 38, wherein the cancer cells are selected from the group consisting of lung cancer cells, prostate cancer cells, multiple myeloma cells, and melanoma cells.